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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,149	06/30/2006	Christopher Robert Bebbington	073678-0026	9929

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EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,149	BEBBINGTON ET AL.	
	Examiner	Art Unit	
	CELINE X. QIAN	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-109* is/are pending in the application.

4a) Of the above claim(s) *65-72,74,78,80-92,94-99,101,102 and 107-109* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-64,73,75-77,79,93,100 and 103-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0507,1107*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 48-109 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 11/12/09 is acknowledged. The traversal is on the ground(s) that claims reciting limitation of UCOE or a cistron encoding an antibody are found in dependent claims of Group I, and claims of Groups II and III recites limitation of that overlap with the claims of Group I. Applicants thus conclude that the claims share unity of invention.

The above argument has been fully considered but it is not found persuasive because the special technical feature of Group I does not make a contribution over prior art according to PCT Rule 13.2. As stated in the previous office action, the special technical feature of Group I is a vector system comprising one cistron encoding an apoptosis protecting protein and another cistron encoding a transactivator, which is demonstrated by WO 03/006607 (see Figure 13 and 14), to lack novelty and inventive step over the prior art. Therefore, this special technical feature cannot link the inventions of Groups I-III as a whole to be a unified invention according to PCT Rule 13.1. As such, for reasons stated in the previous office action and above, the restriction requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 65-72, 74, 78, 80-92, 94-99, 101, 102, 107-109 are withdrawn from consideration for being directed to non-elected subject matter. Claims 48-64, 73, 75-77, 79, 93, 100, 103-106 are currently under examination.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 5/22/07 and 11/2/07 have been considered by the examiner.

Claim Objections

Claims 73, 79, 93 and 100 are objected to because they depend on non-elected claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 48 and 49 are rejected under 35 U.S.C. 102 (a) and (e) as being anticipated by Reff et al (WO 03/006607, IDS).

Reff et al. disclose transforming cells with two vector, one encoding an apoptosis protective protein (Aven or E1B-19K), whereas the other encoding a transactivator (inductive vector pVgRXR). Reff et al. also disclose transforming cells with three vector, wherein one is a transactivator (pVgRXR), the others being an apoptosis protective protein (Aven and E1B-19K), wherein the promoter directs the expression of the apoptosis protein can be activated by the

transactivator (see Figure 13 and 14, and legend). Therefore, Reff et al. disclose the instantly claimed invention.

Claim 48 is rejected under 35 U.S.C. 102(b) as being anticipated by Rao et al (PNAS, 1992. Vol.89, pages 7742-7746).

Rao et al. disclose three vectors, one encoding a transactivator, E1A, the others encoding apoptosis protecting protein, E1B 19K and Bcl-2 protein (see abstract). Therefore, Rao et al. disclose the instantly claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 50-52, 56, 58-64 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reff et al.(IDS), in view of Cockett et al.(IDS) and Rao et al (PNAS, 1992. Vol.89, pages 7742-7746).

Reff et al. teach preventing and delaying apoptosis by expressing one or more anti-apoptotic polypeptides such as E1B-19K and Aven in the cell (see page 5, [0013]), wherein the expression of said anti-apoptotic protein results in the increased production of a cell related product, such as an antibody to anti-CD20 antibodies etc (see page 5, [0014]). Reff et al. teach that such suitable host cells for large scale production of recombinant protein may be CHO cells, BHK cells or COS cells (page 11, [0050]).

However, Reff et al. do not teach expression vector encoding the polypeptide of interest is under the control of a promoter that responds to a transactivator.

Cockett et al. teach vectors expressing adenovirus 5 E1A or mutant are introduced into CHO-K1 cells in order to transactivate the hCMV-MIE promoter. Cockett et al. teach that hCMV-MIE promoter is highly efficient in CHO cells (see page 319, 2nd col., 2nd paragraph, line 1). Cockett et al. demonstrate that E1A protein and its mutant can activate the activity of hCMV-MIE promoter in CHO cells, and increases the production of TIMP in cell culture (see Table 1, and page 321, 1st col., 2nd paragraph). Cockett et al. further teach that high level expression of E1A, however, is toxic to cells (see page 322, 1st col., 3rd paragraph).

Rao et al. teach expression of adenovirus E1A protein renders cell susceptible to apoptosis (see page 7743, 2nd col., 2nd and 3rd paragraph). Rao et al. further teach that expression of E1B-19K and Bcl-2 protects cell from E1A induced apoptosis (page 7743, 2nd col., 4th paragraph, and 7745, Figure 5 and legend).

It would have been obvious to an ordinary skill in the art to transfect a vector encoding a transactivator such as E1A into the recombinant host cell for producing a polypeptide of interest such as a recombinant antibody based on the combined teaching of Reff et al., Cockett et al. and

Rao et al. The ordinary skill in the art would realize the advantage of using such transactivator because Cockett et al. have demonstrated that said protein can transactivate the activity of hCMV-MIE, a promoter commonly used in CHO cells for producing recombinant protein. The ordinary skill in the art would recognize that use of such transactivator at high level may induce apoptosis of the host cell, which is not desirable for producing recombinant protein, and therefore, transfecting a apoptosis protecting protein to overcome such toxicity based on the teaching of Rao et al. Since Rao et al. already demonstrated the feasibility of inhibiting apoptosis by expressing E1B-19K and Bcl-2 in BHK cells, and Reff also demonstrate that expressing E1B-19K and Aven can protect cells from apoptosis in CHO cells, absent evidence from the contrary, the ordinary skill in the art would have reasonable expectation of success to develop a system comprising vectors that express E1A, Bcl-2 and/or E1B, and transfecting them to recombinant protein producing host cells such as BHK or CHO to increase the production of recombinant protein. Using prior art known methods to improve a known system would have been within the capability of an ordinary artisan. Therefore, the claimed invention would have been *prima facie* obvious to an ordinary artisan at the time the invention was made.

Claims 53-55, 57, 73, 75-77, 79, 93, 100, 104-106 rejected under 35 U.S.C. 103(a) as being unpatentable over Reff, Cockett and Rao et al., as applied to claims 50-52, 56, 58-64 and 103 above, and further in view of Antoniou et al (WO 00/05393, see IDS).

The teaching of Reff, Cockett and Rao et al. were set forth above. However, the references do not teach the inclusion of IRES, UCOE, and use retroviral vector.

Antoniou et al. teach the isolation of a polynucleotide comprising a ubiquitous chromatin opening element from hnRNP promoter, which comprises an extended methylation free CpG

island. Antoniou et al. teach that such UCOE maintains stable expression of exogenous gene in recombinant cells (see page 84, lines 1-28). Antoniou et al. also teach the inclusion of IRES in vector for expressing foreign gene (see page 13, line 25), and the vectors may be integration vectors such as retroviral vectors (see page 14, lines 6-15).

It would have been obvious to an ordinary skill in the art to include cis element such as the hnRNP UCOE and IRES to the vector system discussed by Reff, Rao and Cockett for producing recombinant protein, as well as use retroviral vectors in such vector system. The ordinary artisan would have recognize that use of such elements would maintain stable expression of the foreign gene in a host cell (UCOE), and increase the expression of the second gene in the same vector (IRES) based on the teaching of Antoniou et al. Retroviral vectors are widely used for expressing foreign gene at the time of filing. Combining prior art known elements to improve a known system based on their intended function would have been obvious to an ordinary skill in the art. Therefore, the claimed invention would have been *prima facie* obvious to the ordinary artisan at the time the invention was made.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CELINE X. QIAN whose telephone number is (571)272-0777. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Celine X Qian /
Primary Examiner, Art Unit 1636